UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/752,563	01/08/2004	Wolfgang Bergter	1.272.PCTUS.CON	5588

7590 09/08/2006

Gudrun E. Huckett, Ph.D.
Lonsstr. 53
Wuppertal, 42289
GERMANY

EXAMINER	
HORNING, MICHELLE S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/752,563	BERGTER, WOLFGANG	
	Examiner	Art Unit	
	Michelle Horning	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☒ Claim(s) *7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *none*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to communication filed 1/08/2004. The status of the claims is as follows: all claims 1-7 are pending and all claims 1-7 are under current examination.

Information Disclosure Statement

Applicant did not file an Information Disclosure Statement.

Claim Objection

Claim 7 is objected to because of the following informalities: the word "or" is missing. Appropriate correction is required.

Claim Rejections

35 U.S.C. 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1, 3, 4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent # 5, 332, 567 (or "Goldberg" hereafter), and further in view of Gunthard et al and Behr et al.

The limitations of claim 1 are:

1. method of treating viral infections and virally induced tumors comprising

(a) a monoclonal antibody or its antigen binding fragment against a *viral or virus induced antigen* expressed on the plasma membrane of infected cells;

(b) a conjugated radioactive component that is either an alpha or beta emitter; and

(c) the administration of the RIC is after or during an antiretroviral therapy.

Goldberg meets the above limitations by disclosing a method of treating viral infections (for example, hepatitis B and mouse mammary tumor virus, col. 7 and 8) by administering an antibody or antibody fragment conjugated to an alpha-particle (col. 2, Summary of the Invention and col. 18). Other viruses mentioned for targeting, including HIV and HTLV, are described in the columns 7, 18 and 19. The following recitation (col. 3) from Goldberg describes the targeting of a radionuclide/antibody complex to pathogen-associated antigens in his invention. The antigens are further described as being "cell-surface" in columns 8-9, meeting limitation (a) above.

> The present invention resolves many of the problems involved in the treatment of infections that are refractive to conventional drug therapy by using very specific antibodies made against microbial or parasitic antigens in order to target an effective **radionuclide** and/or chemical agent to foci of infection, thereby selectively killing the pathogen. A targeted drug can have enhanced effectiveness due to significantly increased concentration at the target site relative to the rest of the body. **The targeting antibody is able to bind to an accessible epitope of the pathogen or to antigens shed by the pathogen** or resulting from its fragmentation and/or destruction, and which accrete at a focus of infection. The epitope can be on the surface of the pathogen or antigen or at an accessible locus in the pathogen. The therapeutic component of the conjugate is thereby localized at the target site with higher efficiency and an enhanced target to non-target ratio.

Although Goldberg does not specifically teach the use of beta-emitters, beta-emitters in radioimmunotherapy are well described in the prior art. Behr et al describes a comparative study of alpha and beta-emitters in radioimmunotherapy using the human colon cancer model (whole document). Further, the technique of radiolabeling is well

described under Materials and Methods. It would have been obvious to one of ordinary skill in the art to modify the method taught by Goldberg in order to use a beta-emitter conjugated to an antibody or antigen fragment. One would have been motivated to do so, as suggested by Behr et al, in order to characterize and compare the therapeutic efficacy and toxicity of targeted therapy using either alpha or beta-emitters for optimal treatment. There would have been a reasonable expectation of success, given that radioimmunotherapy and all of the underlying techniques are well known and commonly used in the prior art.

Claim 4 is further drawn to frequency of administration as well as the dosage to be administered. However, optimization of drug administration is obvious to one of ordinary skill in the art and Goldberg addresses this in col. 12 in the following recitation:

> Amounts of other imaging radionuclides will be readily determined by the ordinary skilled artisan, by reference to the above isotopes and in view of the half-life of the nuclide and the size of the antibody/fragment/composite to which it is to be conjugated.

Neither of the references mentioned above teach the administration of the RIC subsequent to or during other therapies, for example antiretroviral therapy. It is, for example, well known in the art that antiretroviral treatment suppresses plasma human immunodeficiency virus to levels below the limit of detectability for up to 2 years or more (see introduction of Gunthard et al). As disclosed by Gunthard et al, proviral DNA persists in lymph nodes and peripheral blood mononuclear cells and continues to harbor infectious virus following antiretroviral therapy. Therefore, it would have been obvious to one of ordinary skill in the art to supplement antiretroviral therapy or other therapies with the methods taught by Goldberg and Behr et al for optimal results. One would have

been motivated to do so, as suggested by Goldberg (col. 3), to selectively kill the pathogen housed within infected cells. There would have been a reasonable expectation of success, given that all limitations have been successfully applied to cancer treatment using the exact strategy of the instant application and the techniques are widely used. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goldberg, Gunthard et al and Behr et al and further in view of Molden et al (1997), Icardi et al (1997) and Borghesio et al (1998).

Goldberg discloses applying the method described above to HIV (col. 18), CMV, EBV (col. 19), HBV and HTLV (col. 7). Goldberg et al does not disclose applying this method to HCV, HDV and HHV8; however, the prior art discloses proteins (e.g. receptors) that are associated with these viruses. Molden et al teach a method in which antibodies bind to the IL-6Ralpha and gp130 subunits of the IL-6 receptors (whole document) and "may therefore provide a useful therapeutic target" in combating HHV8 (see discussion). Borghesio et al teaches the use of IgM antibody to HDV, or IgM anti-HD, which binds to hepatitis D antigen (whole document). Lastly, Icardi et al describes antibodies that bind HCV antigens with high specificity (whole document). Of note, there are many more references describing HCV, HDV and HHV8 that would deem the invention of the instant application obvious to one of ordinary skill in the art. One would have been motivated to do so to selectively target infected cells. Thus, the invention as

a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldberg, Gunthard et al and Behr et al and further in view of McDevitt et al (1998), Ehrhardt et al (1998) and Joensuu and Tenhunen (1999). The limitations of the claims are:

1. method of treating viral infections and virally induced tumors comprising

(a) a monoclonal antibody or its antigen binding fragment against a *viral or virus induced antigen* expressed on the plasma membrane of infected cells;

(b) a conjugated radioactive component that is either an alpha or beta emitter; and

(c) the administration of the RIC is after or during an antiretroviral therapy; and

2. wherein the emitters are either alpha or beta, more specifically, emitters listed in claims 6.

As discussed above, limitation #1 has been met. Goldberg further discloses emitters including astatine-211, I-131, Re-186 and Re-188, described in col. 18. McDevitt et al discloses nuclides bismuth-213, radium-223, Tb-149 and actinium-225 (whole document). Ehrhardt et al teaches the use of Lu-177, Rh-105 and Sm-153 (whole document) while Joensuu and Tenhunen teach the use of Sr-89 (whole document). All of the mentioned references describe the use of these radionuclides for therapeutic applications, including radioimmunotherapy. It would have been obvious to one of ordinary skill in the art to modify the methods taught by Goldberg and use

different emitters for radioimmunotherapy. One would have been motivated to do so, as suggested by Ehrhardt et al (see Introduction), since the use of some emitters are limited by the extremely short range of particles in tissue. There would have been a reasonable expectation of success, given that many references describing radioimmunotherapy using many different emitters, both alpa and beta, are well known and successful in the prior art. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michelle Horning whose telephone number is 571-272-9036. The examiner can normally be reached on Monday-Friday, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 570-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for unpublished application is available through Private PAIR only. For more information about PAIR system, see htt://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michelle Horning
Patent Examiner

BRUCE R. CAMPELL, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600